and wherein step (b) comprises

(iv) preparing said compound represented by the model of (ii);

(v) incorporating the compound into an IgE/FcεRIα protein binding assay; and

(vi) assessing whether the compound inhibits binding of IgE to the FcεRIα protein.

A1 Cont

39. (New) The method of Claim 36, wherein the 3-dimensional model of (a) is produced by molecular replacement using atomic coordinates selected from Table 1, Table 2 or Table 3.

REMARKS

Claims 1-20 have been canceled.

New Claims 21-39 have been submitted.

I. Election of Group and Species

In response to the Restriction Requirement mailed July 18, 2002, Applicants provisionally elect to prosecute Group 1 with traverse. Additionally, with regard to election of a species, Applicants elect to prosecute the atomic coordinates of Table 1, again with traverse. Applicants note these elections are made solely in the interest of expediting prosecution of this Application and Applicants reserve the right to traverse division between Groups 2-10 and division between species in subsequent divisional filings. Applicants also reserve the right to file divisional Applications relating to these claims without the need to file a terminal disclaimer.

The Examiner has restricted the present Application into 10 different groups related to three-dimensional models of a human IgE Fc region, methods of producing a crystal of human IgE Fc region, human IgE Fc polypeptide, polynucleotides encoding human IgE Fc region, methods of making human IgE Fc region polypeptide, methods of assaying structures that inhibit binding of IgE and FcεRIα, inhibitors of such binding, methods of improving the function of an antibody, peptide fragments of antibodies that bind FcεRIα and polynucleotides that encode fragments of an antibody that bind FcεRIα. Group 1, consisting of Claims 1-3, is drawn to a three-dimensional models of a IgE Fc region and methods of producing such models. Applicants note Claims 1-20 have been cancelled and new Claims 21-39 submitted. For the Examiners convenience, the chart below relates the subject matter of the previous Claims to the subject matter of the newly submitted claims.

Group	Previous Claim	New Claims	Subject Matter
1	1	21-27	Three- dimensional model of a human IgE Fc region
1	2	30-35	Method to produce a three-dimensional model of a human IgE Fc region
1	3	28-29	Method to produce a three-dimensional model of a FcεRIα binding domain other than a human FcεRIα binding domain
6	12	36-39	Method to use a three-dimensional model of a human IgE Fc region to identify a compound that inhibits the binding of IgE to a FcεRIα protein.

II. Restriction Between Groups 1 and 6

Applicants traverse the restriction between Groups 1 and 6 to the extent that Group 6 requires the use of the subject matter of Group 1. Applicants submit that the subject matter of these Groups is sufficiently small and is so closely related, that a thorough search for Group 1 should also include the subject matter of Group 6. Specifically, the Claims of Group 6 are drawn to a method of identifying a compound that inhibits the binding between an IgE antibody and a FcεRIα protein using the three-dimensional model encompassed by the Claims of Group 1. Applicants emphasize the method defined by Group 6 requires using a model of a protein encompassed by the Claims of Group 1 and, therefore, a search for the subject matter of either Group would be sufficient to examine the Claims of the related Group. Further, because the method of Group 6 cannot be practiced without the three-dimensional model of Group 1, Applicants submit these Groups do not describe independent inventions as described in the M.P.E.P §802.01 and therefore request rejoinder of these Groups.

In view of the foregoing arguments, Applicants respectfully request that the Examiner withdraw the restrictions between Groups 1 and 6. Applicants reserve the right to traverse restrictions between any of the Groups in subsequent divisional applications. Applicants also reserve the right to file divisional applications relating to any and all of these Groups without the necessity of filing a terminal disclaimer.

In any event, if the elected claims of Group 1, are allowable, Applicants reserve their right to amend the claims of Group 6 to be commensurate in scope with the product claims of Group 1, and to request that the claims of Groups 6 that depend from or otherwise include all the limitations of the allowable product be rejoined and examined for patentability. *In re Brouwer*, 37 USPQ2d 1663 (Fed. Cir. 1996); *In re Ochiai*, 37 USPQ2d 1127 (Fed. Cir. 1995).

III. Restriction between Table 1, Table 2 and Table 3

The Examiner has further required Applicants to elect a Table of atomic coordinates for prosecution on the merits. In response, Applicants have elected Table 1 from the grouping of Table 1, Table 2 and Table 3. The Examiner has stated that each Table of coordinates is a patentably distinct specie of the claimed invention to be examined independently. Applicants respectfully disagree noting that each table contains coordinates describing the amino acids from the crystal structure of human IgE. All of the coordinates in these Tables were obtained using IgE having the same amino acid sequence and crystallized in the same way. Applicants therefore submit the coordinates in each of the Tables represent minor variations of the same crystal structure.

The Patent Office may require restriction if two or more "independent and distinct" inventions are claimed in one application. However, "if the search and examination of an entire application can be made without serious burden, the Examiner must examine it on the merits, even though it includes claims to distinct or independent inventions." M.P.E.P Section 803. In the present Application, the coordinates of Tables 1, 2, and 3 represent nearly identical crystal structures so that a search done for one set of coordinates would suffice for the entire group. Because of the high degree of similarity between the crystal structures represented by the coordinates in each Table and the small size of the group to be Examined, Applicants submit that the coordinates of Tables 1, Table 2 and Table 3 can be examined together without serious burden to the Examiner. Therefore, Applicants request withdrawal of the requirement to elect a Table of coordinates for prosecution.

Respectfully submitted,

Dated: September 3, 2002

By: Richard J. Stern

Richard J. Stern, Ph.D.
Registration No. 50,668
Heska Corporation
1613 Prospect Parkway
Fort Collins, Colorado 80525
Telephone: (970) 493-7272
Facsimile: (970) 491-9976

VERSION WITH MARKINGS SHOWING CHANGES

Claims 1-20 have been canceled.

The following new claims have been submitted:

21.(New) A data processing system comprising:

(a) a data storage medium encoding data representing atomic X-ray crystallographic coordinates, wherein said atomic coordinates define the relative position of amino acids from at least a portion of the Cε3 or Cε4 domain from the Fc-region of an IgE protein;

(b) a processing means, wherein said processing means transforms said data into a model representing at least a portion of the Cε3 or Cε4 domain from the Fc-region of an IgE protein.

22.(New) The data processing system of Claim 21, wherein said IgE protein is a human IgE protein.

23.(New) The data processing system of Claim 21, wherein said data represents the atomic coordinates of protein backbone atoms having a root mean square deviation less than 10 angstroms from the human IgE protein Cε3 or Cε4 domain backbone atoms defined by the atomic coordinates represented in Table 1, Table 2 or Table 3.

24.(New) The data processing system of Claim 21, wherein said data represents the atomic coordinates of backbone atoms from a protein having an amino acid sequence at least 80% homologous to the amino acid sequence of SEQ ID NO:2.

25.(New) The data processing system of Claim 21, wherein said data represents at least a portion of the atomic coordinates listed in Table 1, Table 2 or Table 3.

26.(New) The data processing system of Claim 21, wherein said data consists of the atomic coordinates listed in Table 1, Table 2 or Table 3.

27.(New) The data processing system of Claim 21 further comprising a display means for displaying said model.

28.(New) A method to produce a three-dimensional model of the Cε3 or Cε4 domain of the Fc-region of a non-human IgE protein, said method comprising:

(a) obtaining a three-dimensional model of the Cε3 or Cε4 domain from the Fc-region of the human IgE protein using the data processing system of Claim 22;

(b) obtaining the amino acid sequence of a non-human IgE protein;

(c) comparing the Cε3 or Cε4 domain amino acid sequence from the non-human IgE protein with the Cε3 or Cε4 domain amino acid sequence from the human IgE protein;

(d) at positions at which the two sequences differ, replacing the amino acids in the three-dimensional model of the human IgE with the amino acid from the corresponding position of the non-human IgE protein sequence to create a three-dimensional model of the non-human IgE protein; and

(e) displaying said three-dimensional model of the non-human protein on a display means.

29.(New) The method of Claim 28, wherein said three-dimensional model of the human IgE protein is obtained using the atomic coordinates listed in Table 1, Table 2 or Table 3.

30.(New) A method to produce a three-dimensional model of the Cε3 or the Cε4 domain of the Fc-region of the human IgE protein, said method comprising:

(a) obtaining a first set of data representing the atomic x-ray crystallographic coordinates that define the relative position of amino acids from at least a portion of the Cε3 or Cε4 domain from the Fc-region of the human IgE protein;

(b) transforming said first set of data into a second set of data representing a three-dimensional model; and

(c) displaying said data representing said three-dimensional model.

31.(New) The method of Claim 30, wherein the crystallographic coordinates of (a) are selected from Table 1, Table 2 or Table 3.

32.(New) The method of Claim 30, wherein said first set of data is obtained by the steps of:

(i) obtaining a protein crystal comprising at least the Cε3 or at least the Cε4 domain from the Fc region of the human IgE protein;

(ii) producing diffraction data from said protein crystal; and

(iii) transforming said diffraction data into data representing atomic coordinates of said protein comprising at least the Cε3 or at least the Cε4 domain from the Fc region of the human IgE protein.

33.(New) The method of Claim 32, wherein the protein crystal is produced using the hanging drop or the vapor diffusion method, wherein the protein comprising the Cε3 or Cε4 domain from the Fc-region of the human IgE protein is concentrated in a solution comprising about 10 mM Tris-(hydroxymethyl)aminomethane at about pH 8.0, and crystallization is performed using a precipitant composed of about 25 mM sodium acetate at a pH of about 4.6 and 33% polyethylene glycol 4000.

34.(New) The method of Claim 32, wherein the protein crystal belongs to the space group $P42_12$ with unit cell dimensions of a equals about 105 Å, b equals about 105 Å and c equals about 47 Å.

35.(New) The method of Claim 30, wherein said three-dimensional model is displayed as a set of atomic coordinates, a physical three-dimensional model, an image on a computer screen, a picture of said model or a set of coordinates derived from a picture of said model.

36.(New) A method to identify a compound that inhibits the binding between an IgE antibody and a FcεRIα protein, said method comprising:

(a) using a three-dimensional model of the Cε3 or Cε4 domain of the Fc-region from a human IgE protein to identify a compound capable of inhibiting the binding between an IgE antibody and a FcεRIα protein; and

(b) testing said compound in an IgE/ FcεRIα protein binding assay to determine if it inhibits binding of IgE to a FcεRIα protein.

37.(New) The method of Claim 36, wherein the three-dimensional model of (a) is represented by the atomic coordinates listed in Table 1, Table 2 or Table 3.

38.(New) The method of Claim 36, wherein step (a) comprises:

(i) obtaining a 3-dimensional model of the Cε3 or Cε4 domains from the Fc-region of the human IgE protein;

(ii) obtaining a 3-dimensional model of a compound; and

(iii) assessing whether said compound model and said model of the Cε3 or Cε4 domains from the Fc-region of the human IgE protein associate through stable interactions, wherein such interactions indicate the compound is capable of inhibiting the binding of an IgE antibody to a FcεRIα protein;

and wherein step (b) comprises

(iv) preparing said compound represented by the model of (ii);

(v) incorporating the compound into an IgE/FcεRIα protein binding assay; and

(vi) assessing whether the compound inhibits binding of IgE to the FcεRIα protein.

39.(New) The method of Claim 36, wherein the 3-dimensional model of (a) is produced by molecular replacement using atomic coordinates selected from Table 1, Table 2 or Table 3.